

WE CLAIM:

1. A method of automatically determining an electric charge - related characteristic or derived parameter of particles in a dispersion or of a cell wall, comprising having a particle - containing dispersion provided in a cell; illuminating the dispersion with light from a light source; detecting from a detection volume light scattered from the particles; applying an electric field to the dispersion at a first frequency of change of direction of the electric field; applying an electric field to the dispersion at a second frequency of change of direction of the electric field; using first signals detected from the scattered light when the first frequency electric field is applied to provide first values related to the velocity distribution of the particles; and using a second velocity related signal or value derived from scattered light during the time that the second frequency electric field is applied to modify the velocity distribution related values to produce a modified particle velocity-related distribution; and wherein the first frequency is low enough to obtain an acceptable resolution of the distribution of particle velocity - related values.
2. A method according to claim 1 wherein the second frequency is high enough that the second velocity related signal or signals is substantially invariant on the precise position at which the detection volume is located.
3. A method according to claim 1 wherein the modification of the first values using the second signal value substantially compensates the first signal for a shift in value that would otherwise be there.
4. A method according to claim 1 in which the measurement of the mean mobility of a distribution of one or more mobilities made at the high

frequency is used to adjust the spectrum of mobilities measured at the low frequency so that the mean of distribution is made identical or similar.

5 5. A method according to claim 4 in which the adjustment comprises a linear offset of the spectrum.

6. A method according to claim 5 in which the size and magnitude of the offset constitutes a determination of the electro-osmotic flow velocity.

10 7. A method according to claim 1 in which measurements are taken at more than two electric field frequencies.

15 8. A method according to claim 1 comprising taking the measurements from a detection volume that is generally on the central axis of a capillary.

9. A method according to claim 1 in which the first, or low frequency is $1\text{Hz} \pm 1\text{Hz}$.

20 10. A method according to claim 1 in which the second, or high, frequency is at least 40Hz.

25 11. A method of determining the electrophoretic mobility of particles in a dispersion comprising having the dispersion in a capillary cell and taking particle velocity related measurements at a relatively high frequency of reversal of an applied electric field taking particle velocity measurements from the dispersion in the cell at a DC or relatively low frequency of field reversal to enable a relatively high resolution of particle velocity distribution to be obtained in comparison with the
30 resolution that could be obtained using only measurements at the high

frequency of field reversal; and using the high frequency measurements to shift the particle - velocity related distribution spectra obtained at low frequency so that the mean of its low frequency peak or peaks in the low frequency spectra substantially coincide with the position of the means of the corresponding high frequency spectra peaks, thereby producing a translated, modified, spectra substantially equivalent to having peaks of the low frequency shape present at the positions of the equivalent high frequency peaks; and using the modified spectra to determine or indicate the electrophoretic mobility of the particles in the dispersion

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12. A method according to claim 11 wherein the high frequency of reversal of the applied electric field is such that the variation in mean velocity for a particle peak in the particle velocity distribution is substantially invariant with the precise position in the cell from which measurements are taken.

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13. A method according to claim 11 in which the measurement of the mean mobility of a distribution of one or more mobilities made at the high frequency is used to adjust the spectrum of mobilities measured at the low frequency so that the mean of distribution is made identical or similar.

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14. A method according to claim 13 in which the adjustment comprises a linear offset of the spectrum.

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15. A method according to claim 14 in which the size and magnitude of the offset constitutes a determination of the electro-osmotic flow velocity.

16. A method according to claim 11 in which measurements are taken at more than two electric field frequencies.

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17. A method according to claim 11 comprising taking the measurements from a detection volume that is generally on the central axis of a capillary.
- 5 18. A method according to claim 11 in which the first, or low frequency is $1\text{Hz} \pm 1\text{Hz}$.
19. A method according to claim 11 in which the second, or high, frequency is at least 40Hz .
- 10 20. A method of determining electrophoretic mobility values for particles in a dispersion held in a capillary, the method comprising taking particle velocity related measurements at a high enough frequency of electric field reversal such that the effect of electro-osmotic flow of the dispersion is negligible; taking velocity - related measurements at a low
15 enough frequency of field reversal such that electro-osmotic flow has a significant effect on the measured velocities, depending upon where in the cross-section of the capillary is the observed signal - generating region, and providing an offset to the low frequency measurements to offset the
20 effect of the electro-osmotic flow component of the observed low frequency velocities, the offset being derived by using the high frequency measurements.
21. A method according to claim 20 in which the measurement of the
25 mean mobility of a distribution of one or more mobilities made at the high frequency is used to adjust the spectrum of mobilities measured at the low frequency so that the mean of distribution is made identical or similar.
22. A method according to claim 21 in which the adjustment comprises
30 a linear offset of the spectrum.

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23. A method according to claim 22 in which the size and magnitude of the offset constitutes a determination of the electro-osmotic flow velocity.

5 24. A method according to claim 20 in which measurements are taken at more than two electric field frequencies.

25. A method according to claim 20 comprising taking the measurements from a detection volume that is generally on the central
10 axis of a capillary.

26. A method according to claim 20 in which the first, or low frequency is $1\text{Hz} \pm 1\text{Hz}$.

15 27. A method according to claim 20 in which the second, or high, frequency is at least 40Hz.

28. A method of measuring the electrophoretic mobility of a dispersion of particles or cells, the measurement being made at or near to the centre
20 of the cross-section of a capillary cell using an optical technique that can select a sample volume that is a small fraction, typically, 1% of the smallest cross-sectional dimension of the cell and in which the frequency of the applied electric field is varied between high and low levels, high level being the frequency at which the electro-osmosis flow of fluid due to
25 the electric charge on the cell wall is substantially zero at the centre of the cell, and the low level being such that the parabolic flow characteristic of electro-osmosis is substantially fully established.

29. A method according to claim 28 in which the measurement of the
30 mean mobility of a distribution of one or more mobilities made at the high

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frequency is used to adjust the spectrum of mobilities measured at the low frequency so that the mean of distribution is made identical or similar.

30. A method according to claim 29 in which the adjustment comprises
5 a linear offset of the spectrum.

31. A method according to claim 30 in which the size and magnitude of the offset constitutes a determination of the electro-osmotic flow velocity.

10 32. A method according to claim 28 in which measurements are taken at more than two electric field frequencies.

33. A method according to claim 28 comprising taking the measurements from a detection volume that is generally on the central
15 axis of a capillary.

34. A method according to claim 28 in which the first, or low frequency is $1\text{Hz} \pm 1\text{Hz}$.

20 35. A method according to claim 28 in which the second, or high, frequency is at least 40Hz.

36. A method of determining the zeta potential distribution of particles and/or the zeta potential of a cell wall, the method comprising using the
25 method of any one of claims 1, 11, 20 or 28 to provide parameters indicative of the electrophoretic mobility and electro-osmotic velocity of the particles and dispersion, and using those parameters to determine the zeta potential distribution of the particle dispersion and/or the zeta potential of the wall of the cell.

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37. A capillary particle electrophoretic mobility distribution determining apparatus comprising:

a holder for a capillary cell adapted to contain a dispersion;

a light source;

a detector adapted to detect light scattered from a detection zone of the capillary;

electric field generating electrodes adapted to generate an electric field in the region of the detection zone;

a controller adapted to control the electric field applied by the electrodes;

a signal processor adapted to process the signals detected in use by the detector to determine a velocity mobility distribution; and in which

the controller is adapted to apply an electric field at a first, relatively low, frequency and at least a second relatively high frequency, the first frequency being low enough that better velocity distribution resolution is achieved in use than could be achieved at the second frequency, and the second frequency being high enough that the measured velocity distribution is substantially unaffected by electro-osmotic flow; and in which the processor is adapted in use to modify the particle velocity distribution spectrum obtained at the first frequency by shifting it by an offset amount to remove the electro-osmotic velocity, the offset amount being determined using

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information from measurements at both the first and second frequencies of field reversal.

38. Apparatus according to claim 37 in which the detection zone is adapted to be substantially at the centre of the cross-section of the capillary.

39. Apparatus according to claim 37 in which the light source is a laser and laser doppler velocimetry is used to obtain the first and/or second particle velocity distribution.

40. Apparatus according to claim 37 which comprises a capillary cell.

41. Apparatus according to claim 37 in which the high frequency measurements are, in use, used to establish a mean velocity for at least one peak and the mean velocity of the equivalent peak at low velocity is used to determine the offset value (measured mean velocity particle peak at low frequency minus mean velocity of particle peak at high frequency equals the electro osmotic offset).

42. Apparatus according to claim 37 in which the first frequency is 1Hz \pm 1Hz.

43. Apparatus according to claim 37 in which the second frequency is at least 40Hz.

44. Apparatus to claim 37 in which the controller applies a square wave field or a sinusoidal field.

45. Apparatus according to claim 37 in which the detected signals are gated to ignore detected signals generated at a time close to the change of direction of movement of the particles.

5 46. A method of determining charge-related characteristics of either (i) particles in a dispersion, or (ii) the material of a test cell wall, or (iii) particle-cell wall attraction; the method comprising providing a fluid sample having particles in it in a cell having cell walls and applying an electric field which is DC or which alternates direction at a relatively low
10 frequency and taking DC/low frequency particle velocity measurements, and also taking particle velocity measurements when the electric field is applied at a substantially higher frequency; and using both the high frequency and low frequency measurements to determine the charge - related characteristic.

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47. A method according to claim 46 in which the measurements are taken from the centre of the cross-section of a capillary cell.

48. A data carrier embodying a computer programme which when run
20 on a capillary electrophoretic mobility analyser performs the method of claim 1.

49. A data carrier embodying a computer programme which when run
25 on a capillary electrophoretic mobility analyser creates apparatus in accordance with claim 37.

50. A measurement cell suitable for use with a particle characterisation apparatus comprises a sample holder cell and a divider, the sample holder cell having at least a transparent portion and being arranged to hold a
30 dispersion sample, the divider engaging a wall of the cell and dividing a

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sample-holding volume of the cell and extending close to a basal face of the cell.

51. A measurement cell according to claim 50 wherein a measurement
5 region is defined between the divider, and the basal face of the cell.

52. A measurement cell according to claim 50 wherein an a.c. voltage is passed through the dispersion, in use.

10 53. A measurement cell according to claim 50 wherein the cell is used in the measurement of electrophoretic mobility distributions.

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